

WHAT IS CLAIMED IS:

1. An oligopeptide comprising at least about 8 amino acids and less than about 40 amino acids which has an amino acid sequence corresponding to the activation sequence of the extracellular domain of a cell surface receptor.
- 5 2. An oligopeptide according to Claim 1, wherein said oligopeptide has at least about 35% sequence similarity with the sequence of an  $\alpha$ 1-domain of an MHC Class I antigen.
3. An oligopeptide according to Claim 2, wherein said sequence of an  $\alpha$ 1-domain of an MHC Class I antigen is SEQ ID NO:1.
- 10 4. An oligopeptide according to Claim 1, wherein said cell surface receptor is selected from the group consisting of insulin responsive glucose transporter, insulin receptor, leptin receptor, low density lipoprotein receptor, insulin like growth factor receptor, granulocyte colony stimulating factor receptor, interleukin receptors including IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-11, IL-12, IL-13, IL-15 and IL-17
- 15 receptors, human growth hormone receptor, VEGF receptor, PDGF receptor, EPO receptor, TPO receptor, transferrin receptor, prolactin receptor, CNF receptor, T-cell receptor, and epidermal growth factor receptor.
5. An oligopeptide according to Claim 4, wherein said cell surface receptor is human.
- 20 6. An oligopeptide selected from the group consisting of SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; SEQ ID NO:13; SEQ ID NO:14; SEQ ID NO:15; SEQ ID NO:16; SEQ ID NO:17; SEQ ID NO:18; SEQ ID NO:19; SEQ ID NO:20; SEQ ID NO:21; SEQ ID NO:22; SEQ ID NO:23; SEQ ID NO:24; SEQ ID NO:25; SEQ ID NO:26; SEQ ID NO:27; SEQ ID NO:28; SEQ ID NO:29; SEQ ID NO:30; SEQ ID NO:31; SEQ ID NO:32; SEQ ID NO:33; SEQ ID NO:34, and SEQ ID NO:35.
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5 7. An oligopeptide at least about 90% homologous to a sequence selected from the group consisting of SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; SEQ ID NO:13; SEQ ID NO:14; SEQ ID NO:15; SEQ ID NO:16; SEQ ID NO:17; SEQ ID NO:18; SEQ ID NO:19; SEQ ID NO:20; SEQ ID NO:21; SEQ ID NO:22; SEQ ID NO:23; SEQ ID NO:24; SEQ ID NO:25; SEQ ID NO:26; SEQ ID NO:27; SEQ ID NO:28; SEQ ID NO:29; SEQ ID NO:30; SEQ ID NO:31; SEQ ID NO:32; SEQ ID NO:33; SEQ ID NO:34; and SEQ ID NO:35.

10 8. A method of modulating the internalization of a cell-surface receptor containing an activation sequence comprising binding an exogenous compound to said activation sequence.

9. A method according to claim 8 wherein said modulating is inhibiting the internalization.

15 10. A method according to claim 9 wherein said exogenous compound comprises an oligopeptide comprising at least about 8 amino acids and less than about 40 amino acids having an amino acid sequence corresponding to an activation sequence of the extracellular domain of a cell surface receptor;

wherein when combined with a cell expressing said cell surface receptor, said oligopeptide inhibits receptor internalization upon ligand binding.

20 11. A method according to Claim 10, wherein said oligopeptide has at least about 35% sequence similarity with the sequence of an  $\alpha$ 1-domain of an MHC Class I antigen.

12. An oligopeptide according to Claim 11, wherein said sequence of an  $\alpha$ 1-domain of an MHC Class I antigen is SEQ ID NO:1.

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13. A method according to Claim 8, wherein said cell surface receptor is selected from the group consisting of insulin responsive glucose transporter, insulin receptor, leptin receptor, low density lipoprotein receptor, insulin like growth factor receptor, granulocyte colony stimulating factor receptor, interleukin receptors including IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-11, IL-12, IL-13, IL-15 and IL-17 receptors, human growth hormone receptor, VEGF receptor, PDGF receptor, EPO receptor, TPO receptor, transferrin receptor, prolactin receptor, T-cell receptor, CNF receptor, and epidermal growth factor receptor.

14. A method according to Claim 13, wherein said cell surface receptor is human.

15. A method according to Claim 13, wherein said oligopeptide is selected from the group consisting of SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; SEQ ID NO:13; SEQ ID NO:14; SEQ ID NO:15; SEQ ID NO:16; SEQ ID NO:17; SEQ ID NO:18; SEQ ID NO:19; SEQ ID NO:20; SEQ ID NO:21; SEQ ID NO:22; SEQ ID NO:23; SEQ ID NO:24; SEQ ID NO:25; SEQ ID NO:26; SEQ ID NO:27; SEQ ID NO:28; SEQ ID NO:29; SEQ ID NO:30; SEQ ID NO:31; SEQ ID NO:32; SEQ ID NO:33; SEQ ID NO:34; and SEQ ID NO:35.

16. A mammalian cell comprising a modified cell surface receptor, wherein said modification comprises an amino acid sequence substitution, insertion or deletion in an activation sequence of the region of the extracellular domain, and wherein said modified sequence is of at least about 8 amino acids and less than about 40 amino acids.

17. A cell according to Claim 16, wherein said cell surface receptor is selected from the group consisting of insulin responsive glucose transporter, insulin receptor, leptin receptor, low density lipoprotein receptor, insulin like growth factor receptor, granulocyte colony stimulating factor receptor, interleukin receptors including IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-11, IL-12, IL-13, IL-15 and IL-17 receptors, human growth hormone receptor, VEGF receptor, PDGF receptor, EPO

receptor, TPO receptor, transferrin receptor, prolactin receptor, CNF receptor, T-cell receptor, and epidermal growth factor receptor.

18. A cell according to Claim 17, wherein said cell surface receptor is human.

5 19. A cell according to Claim 16, wherein said modification comprises the deletion of all or part of a sequence selected from the group consisting of SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; SEQ ID NO:13; SEQ ID NO:14; SEQ ID NO:15; SEQ ID NO:16; SEQ ID NO:17; SEQ ID NO:18; SEQ ID NO:19; SEQ ID NO:20; SEQ ID NO:21; SEQ ID NO:22; SEQ ID NO:23; SEQ ID NO:24; SEQ ID NO:25; SEQ ID NO:26; SEQ ID NO:27; SEQ ID NO:28; SEQ ID NO:29; SEQ ID NO:30; SEQ ID NO:31; SEQ ID NO:32; SEQ ID NO:33; SEQ ID NO:34; and SEQ ID NO:35.

10 20. A method of determining an activation sequence of a cell surface receptor, said method comprising searching for a region of sequence similarity between said cell surface receptor and the sequence of an  $\alpha$ 1-domain of an MHC Class I antigen.

15 21. A method according to Claim 20, wherein said oligopeptide has at least about 35% sequence similarity with the sequence of an  $\alpha$ 1-domain of an MHC Class I antigen.

20 22. An oligopeptide according to Claim 21, wherein said sequence of an  $\alpha$ 1-domain of an MHC Class I antigen is SEQ ID NO:1.

23. A method for screening for a bioactive agent capable of binding to the activation sequence of a cell surface receptor, said method comprising combining a cell surface receptor and a candidate bioactive agent, and determining the binding of said candidate agent to the the activation sequence of said cell surface receptor.

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24. A method according to claim 23, wherein said determination comprises competitive binding of an oligopeptide according to claim 1.

25. A method according to claim 24, wherein either the candidate bioactive agent or the oligopeptide is labelled.

5 26. A method according to claim 23, wherein said cell surface receptor comprises the full length cell surface receptor.

27. A method for screening for a bioactive agent capable of binding to the activation sequence of a cell surface receptor, said method comprising the steps of:

a) combining

- 10 i) said cell surface receptor;  
ii) a ligand bound by said cell surface receptor; and  
iii) an oligopeptide according to claim 1, wherein said oligopeptide binds to the activation sequence of said cell surface receptor;  
to form a test mixture;

15 b) adding to said test mixture a candidate bioactive agent; and

c) determining the binding of said candidate bioactive agent to said activation sequence.

28. A method according to claim 27 wherein said oligopeptide is labelled.

20 29. A method according to claim 27 wherein said candidate bioactive agent is labelled.

30. A method according to claim 27, wherein said cell surface receptor comprises the full length cell surface receptor.

31. A method for screening for an bioactive agent capable of binding to the activation sequence of a cell surface receptor, said method comprising the steps of:

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- a) combining in a first sample said cell surface receptor, a ligand bound by said cell surface receptor, and an oligopeptide according to Claim 1;  
b) combining in a second sample a candidate bioactive agent, said cell surface receptor, a ligand bound by said cell surface receptor, and an oligopeptide according to Claim 1; and  
c) determining the binding of said oligopeptide to said cell surface receptor in said first and said second samples;

wherein a change in binding of said oligopeptide in said second sample relative to said first sample indicates that said agent is capable of binding to said activation sequence.

32. A method for screening for an bioactive agent capable of binding to the activation sequence of a cell surface receptor, said method comprising the steps of:

- a) combining in a first sample a receptor-derived oligopeptide according to Claim 1, and a bioactive peptide having the sequence of an  $\alpha 1$ -domain of an MHC Class I antigen;  
b) combining in a second sample a candidate bioactive agent, a receptor derived oligopeptide according to Claim 1, and a bioactive peptide having the sequence of an  $\alpha 1$ -domain of an MHC Class I antigen; and  
c) determining the association of said receptor-derived oligopeptide with said bioactive peptide having the sequence of an  $\alpha 1$ -domain of an MHC Class I antigen in said first and said second samples;

wherein a change in said association in said second sample relative to said first sample indicates that said agent is capable of binding said activation sequence of said cell surface receptor.

33. A method according to Claim 31, wherein said sequence of an  $\alpha 1$ -domain of an MHC Class I antigen is SEQ ID NO:1.

34. A method for screening for an bioactive agent capable of modulating the internalization of a type-1 cell-surface receptor, said method comprising the steps of:  
a) adding a ligand bound by said cell surface receptor and a candidate bioactive agent to a cell comprising said cell surface receptor; and

b) determining the effect of the candidate bioactive agent on the internalization of said receptor.

35. A method for screening for an bioactive agent capable of modulating the internalization of a type-2 cell-surface receptor, said method comprising the steps of:

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a) adding a candidate bioactive agent to a cell comprising said cell surface receptor; and

b) determining the effect of the candidate bioactive agent on the internalization of said receptor.

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36. A composition comprising a cell-surface receptor with an exogeneous compound bound to the activation sequence.

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